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Human Immunodeficiency Virus Infection in the United States: A review of Current Knowlege

This MMWR supplement was prepared initially as a report to the President and the Domestic Policy Council and was presented to the Council on November 30, 1987. Introduction

Considerable information is available on the prevalence of infection with human immunodeficiency virus (HIV) in the United States. Less is known about the trends or incidence of the infection. Varied data are available from surveys and studies conducted by state and local health departments, medical centers, and the Public Health Service (PHS) and other Federal agencies. The various surveys and studies differ in sampling, inclusion and exclusion criteria for subjects, rigor of ascertaining risk information, and resulting bias. The results, therefore, cannot always be validly compared. In addition, there are appreciable gaps in the available information, and caution must be exercised in generalizing from what does exist. Nonetheless, a description of the approximate patterns and trends of HIV infection emerges.

This report summarizes published and unpublished information on the status of HIV infection in the United States. The review draws from the following: surveillance data bases maintained by CDC, the National Institute on Drug Abuse (NIDA), the National Institutes of Health (NIH), and the Department of Defense; CDC's ongoing monitoring of published studies; and unpublished data gathered in October 1987 by an epidemiologic team from CDC and NIDA that intensively canvassed health departments, various Federal agencies, blood collection agencies, and medical research institutions. The authors are indebted to the public health officials and medical researchers for their cooperation and willingness to share their data for this review. The surveys and studies cited here are those in which sampling did not include persons specifically seeking to be tested (e.g., no counseling and testing center data are presented) and are limited to those with large enough sample sizes to permit reasonable precision. It is possible that some surveys or studies were inadvertently missed. Every effort has been made to acknowledge the sources of data.

In this document a positive serologic test for HIV is considered indicative of HIV infection, and the terms antibody prevalence and infection prevalence are used interchangeably. Unless otherwise stated, a positive serologic test consists of a repeatedly reactive screening test, such as the enzyme immunoassay (EIA or ELISA), followed by a positive supplemental test, either the Western blot assay or the indirect fluorescent antibody test. Conversion from a negative result on a previous serologic test to a positive result in a subsequent test is considered indicative of new infection. Infection Prevalence among Groups at Recognized Risk Homosexual and Bisexual Men

Homosexual and bisexual men remain the major group at increased risk for HIV infection. Since 1984, 50 surveys and studies in 22 cities in 15 states show prevalence rates ranging from under 10% to as high as 70%, with most between 20% and 50% (Table 1, Figure 1). The highest prevalence rates of HIV infection have been documented for cohorts of homosexual men in San Francisco; otherwise, HIV antibody prevalence varies geographically without major concentration in any one region.

These data probably overestimate the prevalence of HIV infection among homosexual and bisexual men in the study areas since most surveys have been conducted among patients at sexually transmitted disease (STD) clinics. Such clinics serve persons whose sexual behavior has put them at high risk of exposure to various sexually transmitted infections, including HIV infection. Few data are available on the prevalence of infection among homosexual and bisexual men who are not seeking medical care, including those who may be at lower risk of infection.

In collaboration with state and local health departments, CDC is expanding HIV serosurveys among sexually active persons at STD clinics. Intravenous Drug Users

The prevalence of HIV antibody among intravenous (IV) drug users varies markedly by geographic region. In 90 studies in 53 cities in 27 states or territories, rates range from 50% to 60% in New York City, northern New Jersey, and Puerto Rico to predominantly below 5% in most areas of the country other than the East Coast (Table 2, Figure 2).

Most data were obtained from surveys at drug abuse treatment facilities, which primarily treat heroin addicts. Patients undergoing drug treatment are believed to represent only about 15% of the estimated 1.1 million IV drug users in the country. Some evidence suggests that many of those not in treatment are habitual users who may be at even higher risk for HIV infection. On the other hand, the estimated 200,000 intermittent users may have a lower prevalence of infection because of less frequent exposure to contaminated needles or equipment.

Clearly, the problem of HIV infection among IV drug users is severe in some regions of the country, especially the Northeast. Areas that currently have a lower prevalence have the potential for substantial increase in infections among persons who share IV needles and equipment. Moreover, drug-use-associated HIV infection affects more than just the drug users; their sex partners and children are also at risk. IV-drug-use-acquired infection has been the source for most U.S. acquired immunodeficiency syndrome (AIDS) cases contracted through heterosexual contact (these cases reflect HIV transmission patterns a few years ago) and the direct and indirect source for the great majority of perinatally acquired AIDS cases (1). Because of the lengthy incubation period between infection and development of AIDS (median, at least 7 years according to CDC data), the status of IV-drug-use-associated HIV infection in a given area cannot necessarily be inferred from risk factor determination among AIDS cases. HIV surveillance through surveys and studies of IV drug users is essential for targeting and evaluating health education and risk reduction activities.

In collaboration with NIDA and state and local health departments and drug abuse agencies, CDC is increasing the number and the standardization of serologic surveys at drug abuse treatment centers. Hemophiliacs

Before the screening of blood and plasma and heat treatment of clotting factor concentrates became routine in 1985, many persons with coagulation abnormalities requiring IV clotting factor replacement as therapy were exposed to infection with HIV. The high prevalence of HIV infection (Table 3) among the estimated 15,500 persons with hemophilia A or B is uniformly distributed throughout the United States, reflecting the national distribution of the clotting factor concentrates they received before 1985. The studies indicate differences in HIV infection by type and severity of coagulation disorder. Overall, approximately 70% of tested persons with hemophilia A (Factor VIII deficiency) and 35% with hemophilia B (Factor IX deficiency) are seropositive. Because hemophilia B tends to be less severe than hemophilia A, patients with hemophilia B generally need fewer treatments with clotting factor and consequently have had fewer exposures to HIV-contaminated factor concentrates. Since most of the serologic surveys have been done at hemophilia treatment centers, where persons with severe hemophilia are more likely to be encountered than persons with mild disease, the HIV seroprevalence rates probably overrepresent the true rate for hemophiliacs as a group.

All factor concentrates currently manufactured for use in the United States are made from plasma from donors screened for HIV antibody and are heat treated to inactivate the virus. Follow-up studies of seronegative hemophiliacs receiving heat-treated factor concentrates are under way throughout the world. Heterosexual Partners of Persons with HIV Infection or at Recognized Risk

A limited number of studies have been done among persons who are heterosexual sex partners of HIV-infected persons but who have no other identified risk factors for acquiring HIV infection. The prevalence of infection observed among these populations ranges from under 10% to as high as 60% (Table 4). It is not clear whether these differences reflect different levels of infectiousness of source partners from the various risk groups or reflect differences in the frequency or type of sexual exposure, the duration of infection in the source partner, coexisting infection (such as genital ulcers) in one or both partners, or the clinical status of the source partner. Recent evidence suggests that infectiousness increases with the deterioration of the source partner's immune system (2). The relative efficiency of male-to-female versus female-to-male transmission may be an important determinant in rates of heterosexual transmission, but there are not yet sufficient data to definitively evaluate differences (3).

Since persons at recognized risk--bisexual men, IV drug users, and hemophiliacs--are not all infected, their heterosexual sex partners would be expected to have a lower infection prevalence than partners of persons known to be infected. Indeed, limited seroprevalence data from heterosexual partners of high-risk persons of unknown HIV status (Table 5) indicate a somewhat lower risk, ranging from 0 to 11%.

CDC, in collaboration with state and local health departments, is expanding the number of HIV surveys in STD clinics. In part, these surveys will evaluate risk factors in STD patients and should help clarify the level of risk to heterosexual partners of persons at high risk. HIV Infection Prevalence among Selected Segments of the General Population

The general population includes persons at various levels of risk for HIV infection. The following groups for which data are available are drawn from the general population and are biased to different extents. That bias depends both on the degree to which persons at high risk are restricted from or exclude themselves from these groups and on the sociodemographic and geographic composition of the groups. The following discussion summarizes 1) information on HIV seroprevalence among these groups, adjusted where possible by age, sex, and race or ethnicity to be comparable with the general U.S. population and 2) the apparent biases for each group surveyed. Adjustment of data for a group by age, sex, and race does not make it "representative" of the population from which the group is drawn; representativeness is a result of unbiased sampling. Adjustment, however, permits more meaningful comparison of rate data from two different groups. This section deals with the overall HIV seroprevalence among these groups. Geographic and demographic differences within the groups and infection trends over time are discussed later. Since persons at high risk are underrepresented in three of the five groups--blood donors, military applicants, and Job Corps entrants--the detected prevalence of HIV infection among these groups presumably is lower than the true prevalence in the demographic segments of the general population from which they are drawn. Blood Donors

Verbal screening of prospective blood donors for HIV risk factors and the request that persons with such risk factors refrain from donation began in 1983 in an attempt to eliminate donations by persons who possibly had been exposed to the agent causing AIDS. Since early 1985, donated blood and plasma have been screened for HIV antibody, and HIV-infected units have been discarded.

In the highly selected population of blood donors, the prevalence of HIV infection is low, 0.020% for 12.6 million American Red Cross blood donations between April 1985 and May 1987. (These represent about half of all voluntary donations in the United States.) The overall level has declined from 0.035% in mid-1985 to 0.012% in mid-1987, primarily as a result of eliminating previously identified seropositive persons from the donor pool. Donors tested for the first time probably provide the best estimate of the HIV infection prevalence in the segment of the population from which donors are drawn. The overall prevalence among first-time donors in the period 1985-1987 has been 0.043% (provisional data provided by R Dodd, American Red Cross).

The prevalence figure cannot yet be adjusted by age, sex, or race, but rates are much higher for men than for women and higher for blacks and Hispanics than for whites. Despite the selected nature of blood donors with regard to HIV risk factors, 80%-90% of seropositive donors interviewed have recognized risk factors for infection.

CDC, in collaboration with blood collection agencies and state health departments, is expanding the national network of HIV surveillance of American blood donors and is expanding and standardizing the evaluation of risk factors among seropositive donors to monitor trends in HIV transmission among "low-risk" populations. Civilian Applicants for Military Service

Since October 1985, all persons applying for active duty or reserve military service, the service academies, and the Reserve Officer Training Corps (ROTC)--a total of over 600,000 persons per year--are serologically screened for HIV infection as part of their entrance medical evaluation. The Department of Defense shares the resulting statistical data with CDC for HIV surveillance purposes.

Military applicants are interviewed by recruiting officials about drug use and homosexual activity (both of which are grounds for exclusion from entry into military service) before referral for medical evaluation. Potential applicants are informed that they will be screened for HIV antibody. It is expected, therefore, that military applicants who are medically evaluated underrepresent IV drug users and homosexual and bisexual men, as well as persons with coagulation deficiencies.

The crude overall prevalence of HIV infection among the military applicants (N=1,253,768) evaluated between October 1985 and September 1987, is 0.15%. Applicants are largely male and limited in age range. Racial and ethnic minorities are overrepresented. When the crude prevalence rate is corrected to reflect the age, sex, and racial and ethnic composition of the U.S. adult population 17-59 years of age, the prevalence is 0.14%.

As described below, the infection prevalence varies considerably by geographic area, age, sex, and race or ethnicity. From the very limited data thus far available, most HIV-seropositive military applicants interviewed have recognized risk factors for infection, even though persons at increased risk are underrepresented among applicants.

The Walter Reed Army Institute of Research, Department of Defense, in collaboration with CDC and state and local health departments, is undertaking a systematic evaluation of risk factors among seropositive military applicants to monitor trends in the modes of HIV transmission in the general population. Job Corps Entrants

Since March 1987, HIV antibody screening has been required as part of the medical evaluation of new participants in residential training programs of the Job Corps (Department of Labor). No such requirement applies for the nonresidential programs; HIV antibody testing and counseling are offered to, but not required of, nonresidential participants. Job Corps entrants, approximately 60,000 of whom will be serologically screened annually, are disadvantaged youths 16-21 years of age. They are drawn heavily from racial and ethnic minorities and represent both the inner-city and the rural poor. There is no entrance restriction on the basis of sexual orientation or hemophilia. Active IV drug addicts are not accepted in the Corps.

Of the first 25,000 residential Job Corps entrants tested, 0.33% were HIV positive (provisional data provided by C Hayman, Job Corps, Department of Labor). It has not yet been possible to adjust this rate to account for the age, sex, or racial or ethnic composition of the group. Sentinel Hospital Patients

To sample a non-self-selected general population, CDC initiated a network of sentinel hospitals in collaboration with the participating institutions in September 1986. In these institutions, serum or plasma specimens available from patients of all ages who are being treated for conditions not known to be related to HIV are tested for HIV antibody in a blinded, or unlinked, fashion. The blinded approach is necessary to avoid 1) involuntary HIV testing of identifiable persons and 2) a volunteer sample, with all the attendant and uninterpretable self-selection biases. Thus far, results are available for preliminary analysis from four hospitals in the Midwest that participated in the pilot phase.

Based on the first 8,668 test results, the overall age- and sex-adjusted prevalence of infection is 0.32%. By comparison, the prevalence for military applicants from the same four cities, adjusted by age and sex for comparability with the sentinel hospital sample, is 0.11%. Prevalence at the institutions ranges from 0.09% to 0.89%.

Sampling at sentinel hospitals is based strictly on the patient's current clinical condition or clinical service, without regard to risks for HIV infection. Although unbiased in terms of self-selection related to risk factors or known HIV status, the hospital patients sampled do not truly represent their communities because they are sick and because different hospitals serve different segments of the community. Also, the hospital population sampled does not represent the highest-risk patients at these hospitals, e.g., those on infectious disease and cancer services and in the emergency room. In a recent study of critically ill patients at a Baltimore, Maryland, emergency room, six (3%) of 203 patients were HIV antibody positive. Five of these six were gunshot or knife wound victims (4).

The major value of the sentinel hospital network is to monitor change in HIV antibody prevalence over time in a non-self-selected sentinel population, since such change should reflect change in infection level occurring in the community.

In collaboration with state and local health departments, CDC is rapidly expanding the number of sentinel institutions to a target of 40 such sites. In addition, CDC is exploring similar sentinel surveillance in collaboration with such groups as consortia of family practice physicians and laboratories that receive diagnostic specimens from these physicians. Newborn Infants and Women of Reproductive Age

Newborns throughout the country are routinely screened for treatable metabolic disorders by filter-paper blood specimens collected by heel puncture shortly after birth. Methods have recently been developed by the Massachusetts Department of Public Health to test these specimens for HIV antibody (5). Since the tests measure maternal antibody that was passively transferred to the newborn, this approach detects HIV infection among women who have borne live infants. (The risk of HIV transmission from an infected mother to her infant is estimated at 30%-50% (6-10), and HIV antibody in the newborn does not necessarily indicate infection in the child.)

Thus far, filter-paper blood testing of newborns has been conducted only in Massachusetts. Testing is blinded, and the only information currently retained with the specimens is general location of the hospital of birth: inner-city, suburban, or rural. With 30,708 tests in 1986-1987, the weighted average prevalence of infection was 0.21% for childbearing women statewide (provisional data provided by G Grady, Massachusetts Department of Public Health). The prevalence varied from 0.80% for women delivering at inner-city hospitals to 0.09% at suburban and rural hospitals. In comparison, female military applicants from Massachusetts have a crude prevalence of 0.13%. Because the age and race of mothers were not collected in this study, the Massachusetts women's HIV antibody statistics cannot be adjusted for precise comparison with military applicant data.

The data that can be obtained by this method truly represent the population of childbearing women and are unbiased in terms of self-selection or exclusion related to risk factors for HIV infection. (However, childbearing women, are not truly representative of all women or even of all women of reproductive age.) CDC, in collaboration with state and local health departments and NIH, is supporting the application of the filter-paper blood test for HIV surveillance and public health management.

Nationwide, female military applicants have a crude HIV seroprevalence of 0.07%. When adjusted by race and age (to the U.S. population 17-59 years of age), the prevalence is 0.04%.

Information on HIV antibody prevalence is available from 27 studies of women in settings related to women's health and childbearing (Table 6). These studies, conducted in 19 cities or areas in 12 states, were targeted heavily to inner-city areas where appreciable levels of infection were anticipated based on data on AIDS cases and drug use. Except among groups of women specifically known to be at high risk for HIV infection (e.g., drug users), the findings range from a fraction of 1% in most areas to as high as 2.6% in the New York City area and in Puerto Rico. (Rates up to nearly 30% were found among groups of pregnant drug users.) In view of the cities and facilities involved, the rates among women not specifically selected because of high risk may represent the upper range for HIV antibody prevalence among reproductive-aged American women. HIV Infection Prevalence in Special Settings

Prisoners, prostitutes, tuberculosis patients, and college students are unique not only because they represent epidemiologically specialized situations but also because public health approaches for prevention and control of HIV infection among these groups differ from those in the general population or in groups at increased risk. Prisoners

Because of the special public health concerns over homosexual and drug-sharing exposures among prisoners, the HIV infection prevalence in prisons is of particular interest.

Thus far, observed HIV antibody prevalence among prisoners (Table 7) is higher than the prevalence among general population groups, probably because prisoners overrepresent past or current IV drug users. However, except for groups specifically tested because of risk for HIV infection, the prevalence rates for prisoners are considerably lower than those seen for risk groups.

In collaboration with the National Institute of Justice, Department of Justice, CDC will support additional seroprevalence surveys in a number of state and federal corrections systems. Prostitutes

Women who exchange sex for money or drugs are a group of particular concern for HIV infection. (Male prostitutes, whose sexual exposure is predominately with other men, are included with homosexual and bisexual men.) Female prostitutes are at risk of HIV infection and AIDS both because of the IV drug use common among them (income from prostitution being a means of paying for drugs) and because of multiple sexual exposures. In addition, they are a potential source of infection for their babies and for their male clients. The prevalence of HIV infection among U.S. prostitutes was recently summarized (11). HIV antibody prevalence is three to four times higher among prostitutes who acknowledge IV drug use than among those who do not. HIV antibody prevalence tends to parallel the geographic pattern of AIDS case incidence for women, and HIV antibody prevalence is over twice as high for black and Hispanic prostitutes as for white and other prostitutes.

Seroprevalence data on female prostitutes (Table 8) vary from 0 to 45%, with highest rates in large inner-city areas where IV drug use is common. The relative importance of IV drug use versus sexual exposure as the mode of transmission for these women cannot be determined from this review. Regardless of how they acquired their infection, female prostitutes represent a potential source for heterosexual transmission. Tuberculosis Patients

Clinical tuberculosis (TB) can occur as an opportunistic disease in HIV-infected persons who are infected with the tubercle bacillus. For the first time in recent history, TB incidence has risen, most prominently in areas of the country with high levels of HIV infection. Therefore, HIV-infected persons may increasingly be found in clinics treating TB patients. In the one study that was not limited to self-selected groups, 19% of 276 TB patients in Dade County, Florida, were found to be infected with HIV (provisional data provided by D Fertel, Pulmonary Division, Jackson Memorial Hospital). In four other studies of TB patients individually considered at high risk, the HIV seroprevalence ranged from 0 to 50%.

The implications of the HIV antibody prevalence for TB clinic patients relate more to the clinical management of TB patients and the control of tuberculosis in the community than to HIV levels in that community. The high HIV antibody prevalence observed thus far among TB patients reemphasizes the CDC recommendations that TB patients be tested for HIV antibody and that HIV-antibody-positive persons be tested for TB (12). TB clinics provide a good setting for AIDS health education and risk reduction since TB patients are seen frequently over extended periods.

CDC is supporting state and local health departments in rapidly expanding the number of serologic surveys in TB clinics to assess the local prevalence of HIV antibody among TB patients and the consequent need for public health interventions. College Students

College students represent selected subgroups of the general population, limited in age range and socioeconomic level. No restriction generally applies in terms of sexual orientation or hemophilia; however, actively addicted IV drug users are presumably underrepresented. Determining the HIV antibody prevalence among student populations is important because of the focused health-education and risk-reduction needs and opportunities in the college setting. No survey data are currently available from college populations.

CDC is initiating a group of serologic surveys and studies at selected campuses in collaboration with health-care providers for those campuses. Geographic and Demographic Aspects ofHIV Infection Prevalence Geography

The distribution of both AIDS cases and HIV antibody prevalence varies substantially by geographic area. Figures 3 and 4, respectively, show the cumulative AIDS incidence rates per million population by state for AIDS cases as a whole and for cases in heterosexual adults and adolescents only. Figures 5 and 6, respectively, show observed HIV antibody prevalence among military applicants (adjusted by sex) and among blood donors (unadjusted rates).* The general geographic correlation between AIDS incidence and HIV antibody prevalence is obvious, suggesting that case data, which are routinely reported with a high level of completeness (13, 14), still remain a useful indicator of geographic distribution of infection.

The geographic correlation between AIDS case incidence and HIV antibody prevalence among military applicants was demonstrated statistically based on the first 6 months' data from applicant screening (15). The same study demonstrated that HIV antibody prevalence among military applicants is disproportionately higher in urban areas than in rural areas, a finding similar to the striking urban predominance in HIV antibody prevalence among childbearing women in Massachusetts. The same pattern is seen with AIDS cases reported to CDC, with incidence of disease much higher in urban than in rural populations.

The geographic distribution of HIV infection differs among the specific risk groups. Figure 7 maps selected seroprevalence data from Tables 1, 2, and 3. Data for hemophiliacs (hemophilia A) indicate similar high levels of infection regardless of area. The prevalence levels vary more among homosexual and bisexual men, with highest levels observed in California and the Northeast and with somewhat lower levels elsewhere. HIV antibody prevalence among IV drug users varies widely, being highest in the New York City area and in Puerto Rico, moderately high elsewhere on the East Coast and in California, and generally below 5% in most other areas of the country. Age

Like AIDS cases, HIV infection prevalence is at present largely a phenomenon of persons in the sexually active and IV-drug-using age range. This age distribution is repeatedly observed among populations where age-specific data are available (Figure 8). Other than among young children (for whom sufficient data are not yet available), the prevalence of HIV infection first becomes appreciable in the mid to late teens; increases rapidly into the late 20s and early 30s, where it peaks; and then declines in the 40s and 50s. Of significance, the age distribution of AIDS cases is roughly parallel to the HIV antibody prevalence among the population-based groups (military applicants and sentinel hospital patients), following the rise, peak, and fall of HIV antibody prevalence rates by 5 or more years.

Because of the marked difference in HIV antibody prevalence by year of age among young adults, the age composition of groups surveyed for HIV antibody will have a major impact on the net observed prevalence. For this reason, when feasible, it is important to age-adjust or stratify prevalence data from survey populations that are not random in terms of age to permit comparison with prevalence data from other groups. Sex

The cumulative incidence of AIDS cases per million population is 13.0 times greater for males than for females. For AIDS cases among heterosexual adults and adolescents, the ratio is 2.9 to 1, males to females (Table 9). Similarly, for HIV infection this male-to-female predominance is found among military applicants (5.5 to 1), blood donors (4.6 to 1), and sentinel hospital patients (2.3 to 1). (An earlier analysis of military applicants (15) gave a male-to-female prevalence ratio of 2.7 to 1; however, this was based on crude rates rather than the age- and race-adjusted rates cited here.) By contrast, in the one principal risk group that includes women--IV drug users--the prevalence does not differ appreciably by sex. The male-to-female ratio appears to vary geographically, at least for military applicants (15), with ratios approaching 1 to 1 (based on small numbers of women positive) in major city areas. It is unclear whether the low ratio in these areas reflects high rates of self-exclusion from the military by homosexual men, high background rates of IV-drug-use-associated HIV infection or heterosexually acquired infection, or a combination of these. The magnitude of the male-to-female predominance of infection observed among the general population groups probably depends on the relative proportion of homosexual and bisexual men to IV drug users and other persons at risk in the particular group surveyed. Race and Ethnicity

The cumulative incidence of AIDS cases is disproportionately high among blacks (3.0 to 1) and Hispanics (2.6 to 1) compared with whites (Table 10). When homosexual and bisexual men with AIDS are excluded, the ratio of AIDS case incidence is 12.0 to 1 for blacks, and 9.3 to 1 for Hispanics as compared with whites. This racial/ethnic disproportion in HIV antibody prevalence is also observed among blood donors, military applicants, and sentinel hospital patients (Table 10). Even among homosexual and bisexual men and among IV drug users, where race/ethnicity-specific data are available, blacks appear to have higher HIV antibody prevalence rates than whites. Among IV drug users, Hispanics also appear to have higher HIV antibody prevalences than do whites. In a large multicenter study of female prostitutes (11), black and Hispanic prostitutes had a higher HIV antibody prevalence (15.4%) than did white and other prostitutes (6.7%), with a ratio of 2.3 to 1. This racial and ethnic disproportion existed both for prostitutes who used IV drugs (2.5 to 1) and for those who did not acknowledge IV drug use (3.3 to 1).

The reasons for this recurring racial disproportion of infection, whether behavioral or biologic, are not yet apparent. The higher rate of IV drug use among black and Hispanic groups, with consequent greater risk of HIV exposure, is clearly a contributing factor. However, this may not be the only factor since even among IV drug users, the HIV antibody prevalence is racially disproportionate. HIV Infection Prevalence among Heterosexuals Without Acknowledged High-Risk Exposure

Considerable concern has been expressed about the level of HIV transmission among heterosexually active persons in the absence of other known risks in either partner. Currently, the national prevalence of HIV infection among such persons remains very low compared with persons with specific risk behavior or known sexual exposure to persons at increased risk.

In military applicants and blood donors, trends in heterosexually acquired infection can be monitored through interview of seropositives because the background rates of infection associated with high-risk behavior are lower than those in the otherwise comparable segments of the general population.

Thus far, two small studies are available in which seropositive military applicants were interviewed to evaluate risk exposures. In New York City, 83% of 24 seropositive applicants who sought counseling through the health department had recognized risk factors, particularly homosexual or bisexual exposure or drug abuse (16). In Colorado, 11 (92%) of 12 seropositive persons had risk factors (provisional data provided by B Dillon, N Spencer, Colorado State Health Department). In a slightly different population, seropositive active-duty military personnel in Colorado, 91% of 33 interviewed men had recognized risk factors (17 and provisional data provided by J. Potterat, El Paso County Department of Health, Colorado). Too few seropositive women were available in any of the follow-up studies for analysis. The Department of Defense, in collaboration with CDC and state and local health departments, is developing a program of interview evaluation of risk factors among seropositive applicants. Heterosexual transmission is most likely to occur in areas with highest rates of AIDS and HIV infection among IV drug users.

Among blood donors, follow-up interviews of seropositive persons have found a large proportion with recognized HIV infection risk factors. In a study in Los Angeles, Baltimore, and Atlanta, 82% of 186 seropositive donors studied thus far have risk factors (provisional data provided by American Red Cross and CDC), as do 86% of 118 seropositives in three Red Cross regions (provisional data provided by A Williams, American Red Cross), and 89% of 109 in the New York City area (provisional data provided by PD Cleary, New York Blood Center).

CDC is collaborating with blood collection agencies and state health departments to develop a network of at least 20 centers where systematic evaluation of risk factors among seropositive donors is conducted.

If the additional planned studies are consistent with these observations, as few as about 15% of currently infected military applicants and blood donors may have acquired their infection heterosexually. This figure corresponds with an estimate of heterosexually acquired infection of 0.021% for applicants (sex-, race- and age-adjusted) and 0.006% for donors. Further risk factor evaluations are needed among seropositive persons from these groups to monitor trends in heterosexual HIV transmission.

Another approach to monitoring for heterosexually acquired infection is measuring the HIV antibody prevalence among patients in STD clinics who, through interview, are carefully determined not to have recognized sexual, IV-drug-related, or blood- or blood-product-related risk factors. STD clinics see heterosexuals whose sexual behavior puts them at highest risk of HIV infection as well as other sexually transmitted infections. Thus, non-IV-drug-using patients at STD clinics make up the most likely subpopulation of heterosexuals in which to observe HIV infection, and HIV antibody prevalence in such patients should represent the highest prevalence and serve as an early warning system for HIV transmission among non-IV-drug-using heterosexuals in a given geographic area. In nine surveys in six major cities, where HIV infection risk was evaluated rigorously through interview with the opportunity to reinterview seropositives, infection prevalence ranged from 0 to 1.2% among persons without identified risk factors (Table 11). Where risk was evaluated less rigorously through an anonymous self-administered questionnaire, a prevalence as high as 2.6% was observed among persons not acknowledging risk. In simultaneous surveys of homosexual patients at these same clinics, the HIV antibody prevalence ranged from 12% to 55%.

CDC is collaborating with state and local health departments to widely expand the serosurveys in STD clinics, including the rigorous evaluation of HIV infection risk factors among heterosexual patients.
HIV Infection Trends Over Time and Incidence of New Infection

Trend and incidence information is much less available and much more difficult to develop than prevalence data. Prevalence trends can currently be observed among large groups that routinely have been screened for at least 2 years, namely, military applicants and blood donors. The other regularly screened general population groups, sentinel hospital patients and Job Corps entrants, have not yet been evaluated long enough to permit a meaningful analysis. Incidence, or the rate of new HIV infection, is measured directly among groups in which the same persons are tested more than once. Currently these groups include active-duty military personnel, repeat blood donors, and recruited cohorts of persons at increased risk.

In the first 24 months of serologic testing of military applicants, the HIV infection prevalence has remained stable, with no statistically significant trend upward or downward for applicants as a group (Figure 9) or when analyzed by sex, age group, race or ethnicity (Figure 10), or geographic region. These trend data should be viewed with some caution. Progressively increasing rates of self-deferral by persons knowing or suspecting they were infected might have masked an increase in prevalence in the population from which military applicants are drawn. However, the data do not suggest an explosive rise in infection in the population from which applicants are drawn, nor do they indicate that new infection has stopped occurring.

Seroprevalence among Red Cross blood donors as a group has progressively declined from an initial 0.035% in mid-1985 to 0.012% in July 1987 (Figure 11). However, this is due to the progressive elimination from the repeat donor pool of persons who had previously tested positive. Data obtained only from first-time donors indicate a prevalence that varies seasonally but that over a 24-month period has shown no upward or downward trend (Figure 12). The peak in seroprevalence seen in mid-summer corresponds to the seasonal change in the composition of the donor pool. In mid-summer, student donors are not available, and the remaining donors tend to be older and drawn more heavily from workforce groups (provisional data provided by RY Dodd, American Red Cross). Similar mid-summer peaks were observed for hepatitis B surface antigen among blood donors in the period 1975-1977 (18).

(Hepatitis B virus infection shares many epidemiologic characteristics with HIV infection.)

Stable observed prevalence levels do not imply absence of new infection. On the contrary, in the age-specific data from military applicants, for example, 20-year-olds in early 1987 had higher rates than 19-year-olds in early 1986; this suggests that new infection continues to occur. Preliminary analysis by birth-year cohort for applicants 17-25 years of age suggests incidence rates for new infection of 0.5 per 1,000 per year for men and 0.1 for women (provisional data provided by JF Brundage, Walter Reed Army Institute of Research). Among 132,920 active-duty military personnel who have been serologically tested more than once, the preliminary rate of 0.77 new infections/1,000 persons/year (0.077%) has been observed (provisional data provided by J McNeil, Walter Reed Army Institute of Research). Among over 3 million donors whose blood has been tested more than once in the American Red Cross system, new infections are also currently observed at the preliminarily estimated rate of 0.003% per year (provisional data provided by RY Dodd, American Red Cross).

While evidence from screening military applicants and personnel and blood donors indicates that new infections continue to occur, several sources of information suggest that the rate of new infection (incidence) may have slowed from previous years in some groups. First, data from eight cohorts of homosexual and bisexual men show progressive declines in the rate of new infection (Table 12, Figure 13). Nevertheless, although lower than in the early 1980s, these rates remain appreciable. Second, the net seroprevalence levels have remained stable for blood donors and military applicants for the past 2 years, suggesting that the incidence of new infection may no longer be high enough to raise the prevalence of HIV infection. Third, because of the behavioral and serologic screening of blood and plasma donors and the heat treatment of factor concentrates, since 1985 the rate of new infection among transfusion recipients and hemophiliacs has been vastly reduced.

The epidemic of HIV infection and AIDS is a composite of many individual, though overlapping, smaller epidemics, each of which has its own dynamics and time course. Whereas the incidence of new infection overall and the incidence among certain subgroups may have declined somewhat, in the absence of specific information, incidence rates cannot be assumed to have declined among all subgroups or in all geographic areas. The HIV infection trends for IV drug users and heterosexually active persons, and for localized areas such as inner-cities, remain of considerable concern. Two studies among originally seronegative IV drug users in the New York City area showed conversion to positive in 3% and 19%, respectively, between 1985 and 1986 (19, 20). Clearly, individuals continue to become infected. There is insufficient information to speculate yet about the overall trend of the epidemic of HIV infection. Implications for National Estimate of HIV Infection Prevalence The Public Health Service Estimate Approach Reconsidered

In May 1986, during the PHS AIDS Planning Conference at Coolfont, West Virginia, a group of public health experts estimated the number of HIV-infected persons in the United States to be from 1 million to 1.5 million. Prior to this time, scientific speculation had focused on HIV infection levels several fold greater than this, and no consensus had been attempted. These nearly 100 experts developed their working estimate based on the estimated size of populations at increased risk multiplied by the corresponding estimates of HIV antibody prevalence from the limited data then available (Table 13). The group expressed concern about the uncertainty of the size of populations at risk. The estimate of 1-1.5 million was consistent with what was then known about the progression of HIV infection to AIDS (20%-30% in 5 years) and the projected cumulative incidence of AIDS (270,000 diagnosed by the end of 1991). The Institute of Medicine, National Academy of Sciences, subsequently reviewed the PHS working estimate and considered it reasonable for planning purposes (21).

Since 1986, additional data have become available on seroprevalence among risk groups and among other populations, and estimates of the size of two of the risk groups have been modified. Based on the

1986 and 1987 seroprevalence observations, the average estimated antibody prevalence can be adjusted from a range of 15%-20% to the range of 20%-25% for exclusively homosexual men, from 10% to 5% for bisexuals and men with infrequent past homosexual exposures, and from 30% to 25% for heavy users of IV drugs; the rate of 35% can be used for hemophilia B patients. NIDA currently estimates there are 900,000 heavy users of IV drugs and 200,000 occasional or intermittent users (provisional data provided by NIDA). There are an estimated 12,400 hemophilia A patients and 3,100 hemophilia B patients (provisional data provided by Host Factors Division, Center for Infectious Diseases, CDC, and the National Hemophilia Foundation). For heterosexual adults 15-59 years of age without specific identifiable HIV infection risk factors, the population figure 142 million was used based on the 1985 U.S. Census estimate of 148 million less the totals for persons at higher risk in the table. The HIV antibody prevalence in this last population group is difficult to estimate with the limited data available, but among interviewed seropositive blood donors and military applicants, less than 15% of total infections occurred in persons with no identifiable risk factors. Therefore, 15% of the age-, race-, and sex-adjusted rate for military applicants, or 0.021%, was selected as the HIV antibody prevalence for this group. For the other groups (heterosexual partners of persons at high risk, heterosexuals born in Haiti and Central Africa, transfusion recipients, etc.) no estimates of population size or seroprevalence are available; however, data from AIDS case surveillance suggest that this miscellaneous group may account for as many as 5%-10% of total infections.

The estimate obtained by incorporating these revisions into the 1986 calculation (Table 14)--945,000 to 1.41 million--differs little from the earlier figure. The major limitation of both the original and the reevaluated estimate is the unknown size of the population of homosexual and bisexual men and the distribution within this population of the frequency and type of risk activity. In view of the limited impact of the new data and population size estimates, modifying the overall PHS working estimate for HIV infection in the United States does not appear warranted at this time based on this approach.
Extrapolation from Observed Rates

What if the seroprevalence or a multiple thereof from the only large currently observed groups, blood donors and military applicants, is used to estimate a national number of infected persons? The prevalence for first-time-tested donors, 0.043%, multiplied by the size of the population 15-59 years of age, 148 million, gives a national figure of 64,000. This is clearly an underestimate since persons at recognized high risk are largely excluded from the blood donor pool. (There also have been 48,000 AIDS cases reported as of early December 1987.) The adjusted prevalence for military applicants of 0.14% multiplied by the size of the population 15-59 years of age gives an estimate of 207,000, also undoubtedly an underestimate because of the underrepresentation of persons at risk of HIV infection in the military applicant pool. Preliminary data from other populations, including Massachusetts childbearing women and patients in sentinel hospitals, provide antibody prevalence estimates two to three times as high as those for military applicants from the same geographic areas. However, even a threefold multiple of the applicant prevalence-based extrapolation, 621,000, is well below the PHS estimate. More representative antibody prevalence information will be needed for a more precise estimate made by this approach. Estimates from AIDS Surveillance Data

Several investigators have suggested that the number of persons infected with HIV can be estimated from data on reported AIDS cases in combination with data on the rate at which infected persons progress to AIDS (22-24). These approaches were considered in some detail at the October 15-17, 1987, workshop on mathematical modeling of AIDS and HIV infection sponsored by the Institute of Medicine, National Academy of Sciences. A variation of this technique is discussed below.

In all of the methods, the number of AIDS cases diagnosed each year can be calculated as the convolution of the number of persons infected in each preceding year and the number of those expected to be diagnosed with AIDS. For this discussion, let $a(t)$ be the number of AIDS cases diagnosed in year t (t=1978, 1979, ..., 1987), let i(t) be the number newly infected in year t, and let d(x) be the proportion of infected persons expected to develop AIDS after x years (x=0,1,2...); then:

The number of AIDS cases per year, a(t), is known from surveillance data and the disease progression rates, d(x), with accompanying 95% confidence bounds have been estimated from a prospective study of HIV-infected homosexual men in San Francisco. It is possible to estimate the number of persons infected, provided specific assumptions are made about the shape of i(t). Three different distributions for the infection curve were considered as follows: logisticI(t)=1/(1+k exp(-rt));log-logisticI(t)=1/(1+(rt)k); anddamped exponentialI(t)=k exp(rtx). Three different sets of progression data, d(x), were also considered: one representing the best estimates from the cohort data, one representing the lower 95% confidence bounds (slowest rate of disease progression), and one representing the upper 95% confidence bounds (fastest rate of disease progression).

AIDS cases reported to CDC through November 2, 1987, were used in the analysis. The totals were adjusted for reporting delays to give the number of diagnosed AIDS cases each year through 1987. The parameters in the different infection curves and the total infections through 1987 were estimated from equation 1 using weighted nonlinear least squares methods. The final estimates were adjusted for underrecognition and underreporting of AIDS cases. Validation studies done in five major U.S. cities in 1985 suggested that 20% or more of AIDS cases were either not reported to health departments or not diagnosed by a method that would allow them to be counted under the AIDS surveillance definition used before September 1987 (13, 14). Variations over time in the completeness of reporting (such as missing a large number of early AIDS cases) would also influence the projected number of cases, but were not considered in these analyses.

The resulting estimates for the cumulative number infected by the end of 1987 are shown in Table 15. The range of estimated values is large, from 276,000 to 1.75 million persons infected, reflecting both uncertainty in the progression rate for AIDS and the varied assumptions about the shape of the underlying infection curve. With use of only the best estimate of the disease progression rate from the San Francisco prospective study, the range of estimates is smaller, from 420,000 to 1.65 million.

These estimates must be evaluated in light of the assumptions made in the models about the shape of the curve and, hence, the spread of the infection. The logistic curve assumes that the spread of infection is limited to a closed group and that all persons in that group have an identical, constant risk for infection. The model does not take into account the addition of persons who are newly at risk; for example, persons who only recently became sexually active or started using IV drugs. The logistic model also assumes that likelihood of transmission is the same for all those at risk, whether they are homosexuals, IV drug users, hemophiliacs, transfusion recipients, or heterosexual partners of infected persons, and that this risk is constant over time. As a consequence of these highly implausible assumptions, the fitted model indicates that virtually all those who will ever become infected with HIV were already infected by 1984. Current data show that substantial numbers of new infections continue to occur in all population groups except hemophiliacs and transfusion recipients. For all these reasons, the logistic model is inappropriate and will severely underestimate the total number of persons now infected.

Although the log-logistic model also assumes a closed group at risk, it allows for a relative slowing in the rate at which the virus is spreading. Such a slowing would be expected for two reasons. First, persons are not homogeneous but have considerably varied risk. Risks will vary by type of exposure (e.g., homosexual, IV drug use, heterosexual, etc.) and by the frequency of exposure. Particularly in a closed or relatively closed group, those at highest risk would have become infected earliest in the epidemic, while the virus might later spread more slowly among those at lower risk. Second, prevention and education efforts would slow the rate of infection; however, some would argue that since the major groups at risk are not really "closed," the increasing prevalence of HIV infection could lead to increased spread simply because more infected persons are available to transmit the infection. The log-logistic model is much more appropriate than the logistic, but will likely still underestimate the eventual number of persons who will become infected with HIV.

The third model, the damped-exponential, also allows for a relative slowing in the rate at which the infection is spread, but does not assume that the population at risk is closed. On the contrary, it assumes that the number of potential HIV infections is limitless. While such an assumption may be unreasonable over the long term, it may accurately represent the short-term spread of HIV among populations in which prevalence is low and/or the number of persons entering the risk groups exceeds or equals the number becoming infected.

Both the log-logistic and the damped-exponential models fit the AIDS surveillance data well, and their curves have similar shapes in the early stages of the epidemic, but diverge rapidly beyond 1984 because of their different underlying assumptions. Since very few persons infected with HIV progress to AIDS during the first 2-3 years, AIDS case data alone cannot determine which of these models is more appropriate and, hence, what is currently happening with regard to HIV infection. Rather, the AIDS cases seen today reflect primarily trends in infection through and including 1984, before current prevention activities, such as screening of blood donations, testing and counseling efforts, and information and education activities began. For example, application of the damped-exponential model to surveillance data for transfusion-associated cases would lead to the erroneous conclusion that HIV has spread rapidly in the blood supply since 1984, while application of the log-logistic model to the same data in 1985 would have been falsely reassuring at that time before blood donations were screened for HIV antibody.

It is unlikely that any one of these models accurately describes the transmission of HIV within the population. Many different models are consistent with currently available AIDS surveillance data, and these data alone are not sufficient to determine the extent of HIV infection.* Procedures that produce such a wide range of results from the same data indicate that there are insufficient data or insufficient models or both. Implications

The estimation of a total number of infected persons remains complex and inexact. The approaches described for computing or recomputing a national HIV antibody prevalence cannot be considered definitive. The results, however, are consistent with the previous PHS working estimate of 1-1.5 million. None of the above approaches indicate that the estimate is too low or too high, and the available data and mathematical models do not currently warrant a change in the estimate. Since some HIV transmission clearly has occurred in the past 17 months, the 1.5 million upper limit of the original estimate may have been high when it was made. There is no substitute for carefully obtained HIV antibody incidence and prevalence data. Observations and Comments

This review of the extent and trends of infection with HIV in the United States is necessarily descriptive and qualitative. The marked variability in study design, sampling, and biases among the available serologic surveys and studies makes quantitative comparisons only approximate. Nevertheless, the picture emerges of extensive HIV infection among the recognized risk groups of homosexual and bisexual men, IV drug users, hemophiliacs, and the heterosexual partners of these persons. Exclusively heterosexual persons who do not abuse drugs and who are not knowingly the partners of persons with or at risk of HIV infection are much less likely to be infected. However, no infection trend information is yet available to evaluate whether the risk is rising for this latter group.

With few exceptions, HIV antibody prevalence among observed groups from the general population, which includes high-risk as well as low-risk persons, is a fraction of 1%. At this time, HIV infection, like AIDS, occurs primarily among young to early-middle-aged adults; insufficient information is available on young children. In general, males are much more likely than females to be infected, and blacks and Hispanics more likely than whites. Geographic differences in infection prevalence remain consistent with the distribution of AIDS cases. While new infections continue to occur, the rate of new infection among several groups, including homosexual men, appears to have declined; this decline may have major implications for the overall incidence of new infection, since homosexual men have been the largest group at risk for HIV infection. Information is not yet sufficient to evaluate infection trends for IV drug users, heterosexually active persons, or specific geographic areas.

Many gaps in knowledge remain. More precise and more consistently collected data on the prevalence of HIV infection must be collected for the recognized risk groups, for heterosexually active persons, and for accessible segments of the general population. Better and more extensive information is essential for targeting and evaluating control and prevention efforts at local and state levels, for predicting future health-care needs, and for understanding where the HIV and AIDS epidemic is headed. Better models using the specific data will also aid in our understanding of the spread of this virus. Surveillance of the prevalence and incidence of HIV infection by continual monitoring of sentinel populations and expansion of focused seroprevalence surveys and studies, as well as development of models to help interpret the data, remain critical elements of the nation's response to this major public health crisis. ackAcknowledgments

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